America's Blood Centers

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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Reference: **Docket No. 99D-2213: Draft *Guidance for Industry: Revised Recommendations for the Invalidation of Test Results When Using Licensed and 51 O(k) Cleared Bloodborne Pathogen Assays to Test Donors"***

To Whom it May Concern:

America's Blood Centers appreciates the opportunity to comment on the Center for Biologics Evaluation and Research's recent draft guidance on invalidating test results when using bloodborne pathogen assays. In general, we believe this guidance helps reconcile previous inconsistencies between CBER regulations and the Health Care Financing Administration's CLIA regulations.

We have the following specific comments:

Section II (Background) (Paragraph 1). The draft guidance notes that the Centers for Disease Control and Prevention has determined that a test-kit supplied "control" reagent" may serve as a calibrator or a control reagent but cannot serve as both simultaneously. Since the test kit manufacturers tend to use the term "control" broadly, there is considerable room for misinterpretation. We suggest that the test kit manufacturers be required to specify more precisely in their labeling the exact purpose or function of included "controls" (i.e., whether they perform the function of control and/or calibrator).

Section III A. We are seeking clarification about the intent of the last sentence of the section, which says: "prior to implementation, additional control reagents should be qualified to minimize possible incompatibilities that may exist with particular test kits." We request that CBER further define the word "qualified" to specify how qualifying will be done and who will do it (e.g., the control manufacturer, the kit manufacturer or the user).

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Section III A (Table). We suggest that both a Negative and a Positive external control be required when individual Negative controls supplied by a test kit are used in calculating the cutoff.

> We believe that requiring only an additional Negative external control to be run with a test kit's Negative control is insufficient In general, the main difference between a positive and negative control is the constituent to be measured (either present in the positive control or absent in the negative control). The controls must have the same suspension media, the same viscosity, the same pH, the same osmolarity, etc. This does not seem possible if the assay run is limited to test kit controls, samples and an additional negative control.

Section III C. We suggest rewording the last sentence of the first paragraph as follows:

> **"Invalidated non-reactive specimens should be re-tested singly, and those results, if valid, should become the test of record."**

The language in the draft says, "Invalidated non-reactive specimens should be retested singly and those results become the initial test of record" is confusing. Should the retest also be invalid, then the test of record would be an invalid result. The use of the word "initial" associated with "'test of record" implies initially reactive.

Section HI, C. We request deletion of the last sentence of the second paragraph in this section, which requires completion of all aspects of investigation, corrective action, documentation, and supervisory oversight before an invalidated test of a sample or set of samples can be re-run.

> **This requirement is excessively time-consuming and will delay the completion of necessary testing. Moreover, we believe it goes beyond HCFA's CLIA regulations**

If you would like to discuss the above questions further, I can be reached at (302) 737-8405, ext. 767.

Yours truly,

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